California Antimicrobial Resistance Laboratory Network: *Candida auris*: Emergence, Laboratory Identification, and Public Health Response

June 27th, 2017
Candida auris: Emergence, Laboratory Identification, and Public Health Response

• Describe the epidemiology of C. auris

• Discuss infection control and public health response to C. auris cases

• Describe laboratory considerations for C. auris identification

• Discuss role of the California AR Lab Network in C. auris surveillance
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Candida auris Emergence, Laboratory Identification, and Public Health Response

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Mycotic Diseases Branch, Centers for Disease Control and Prevention
CA DPH Webinar
6/27/2017
What the public thinks
What the healthcare professionals think
THERE'S A FUNGUS AMONG US.
Fungi can cause serious, invasive infections and be HAIs

- **Candidemia**
  Most common healthcare-associated BSI in a recent US point prevalence study
- **Incidence of 5-15/100,000**
- **30-50% mortality**

Magill et al, Multisite point prevalence survey of HAIs, NEJM 2012
Risk Factors for Candidemia ("the other C. diff")

- Broad-spectrum antibiotic use
- Immune compromise
- Prolonged ICU stay
- Abdominal surgery
- Central lines
Source of infection

- **Conventional wisdom:** autoinfection with host gut flora
- Transmission in hospital environments not thought to be common
- Outbreaks rare
Bloodstream *Candida* species distribution, EIP Surveillance, U.S. 2008-2016 (n=~7000 isolates)
Why We Care About an Obscure Candida Species called *C. auris*
It always starts with an email...

February 2015

- Pakistani colleagues concerned about outbreak of *Saccharomyces cerevisiae* infections
  - 22 isolates over 2 months
  - 8 bloodstream, 3 burn wounds, 10 urine, 1 catheter tip
But it wasn’t *Saccharomyces*...

- A commercial test kit had been used for identification
- DNA sequencing revealed that the isolates were *Candida auris*
Discovery of *C. auris*—2009

**Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital**

Kazuo Satoh, Koichi Makimura, Yayoi Hasumi, Yayoi Nishiyama, Katsuhisa Uchida and Hideyo Yamaguchi

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*Auris* is Latin for ear
Rapid Emergence Since 2009
Bloodstream infections, drug resistance

Pakistan
Venezuela
Israel
U.K.

Japan
South Korea
India
Kenya
Kuwait


First report of *Candida auris* in America: Clinical and microbiological aspects of 18 episodes of candidemia


*Candida auris* Candidemia in Kuwait, 2014
Muha Emura, Shuhil Ahmad, Ziaeddin Khair, Leena Joseph, Ina'm Al-Otaibi, Prabhodh Punjabi, Ritu Bafna

*Candida auris*-Associated Candidemia, South Africa
To the Editor: We noted the report by Chouhalary et al. (1) and report *Candida auris* as a cause of candidemia in South Africa.
Cryptococcus neoformans
Rhodotorula glutinis
Candida rugosa
Candida krusei
Candida lusitaniae
Candida auris
Candida haemulonii
Candida duobushaemulonii
Candida pseudohaemulonii
Saccharomyces cerevisiae
Candida glabrata
Candida bracarensis
Candida nivariensis
Candida catenulata
Candida pelliculosa
Candida albicans
Candida dubliniensis
Candida tropicalis
Candida metapsilosis
Candida parapsilosis
Candida orthopsilosis
Candida famata
Candida fermentati
Candida guilliermondii

Closely related to other *Candida* species known for antifungal resistance

*Candida auris* likes high salinity, high temperatures (>40°C)
CDC Formed an International Collaboration
Major antifungal resistance was seen

- 93% resistant to fluconazole
- 54% resistant to voriconazole
- 7% resistant to echinocandins
- 35% resistant to amphotericin B
- 41% isolates multidrug resistant
- 4% resistant to all three classes
By way of comparison: *Candida glabrata*

- 1-3% isolates multidrug resistant
- 0 pan resistant isolates

1. 11% resistant to fluconazole
2. 1-6% resistant to echinocandins
3. <1 % resistant to amphotericin B

- 1-3% isolates multidrug resistant
- 0 pan resistant isolates
Healthy Skepticism

- Was *C. auris* with us all along?
- Maybe newer diagnostic methods responsible for supposed emergence
  - MALDI-TOF
  - DNA sequencing
- Most systems misidentify as *Candida haemulonii* or other species
Not Just Improved Detection

- EIP Candidemia Surveillance Program
  - No *C. auris*

- SENTRY and ARTEMIS programs (private collections from 4 continents)
  - >30,000 *Candida* isolates from 1996-2015
  - No *C. auris* before 2009

- Earliest known isolate of *C. auris* has been recorded in S. Korea in 1996
How Did *C. auris* Emerge?

- Global spread of single epidemic strain? (e.g., through food or medical product)
- Many introductions from the environment or other sources?
- Whole-genome sequencing (WGS) provides remarkable but puzzling results
WGS of 47 isolates from 4 world regions

- Very different across regions (>40K-400K SNPs)
- Nearly identical within regions (<70 SNPs)
WGS relationships among Indian/Pakistani strains

But only 70 SNPS within the groups
But This Really Got Our Attention...

- *C. auris* outbreak in a UK hospital
- 9 *C. auris* bloodstream infections
- >40 people colonized
- Clear patient-to-patient transmission
Hard to Control

- Contact precautions
- Screening for colonization
- Chlorhexidine bathing
- Cleaning room with bleach 3X/day
- Terminal cleaning with higher concentration bleach
- Eventually closed unit

*C. auris* cultured from many hospital surfaces
Global Emergence of Invasive Infections Caused by the Multidrug-Resistant Yeast *Candida auris*

**Summary:** The Centers for Disease Control and Prevention (CDC) has received reports from international healthcare facilities that *Candida auris*, an emerging multidrug-resistant (MDR) yeast, is causing invasive healthcare-associated infections with high mortality. Some strains of *C. auris* have elevated minimum inhibitory concentrations (MICs) to the three major classes of antifungals, severely limiting treatment options. *C. auris* requires specialized methods for identification and could be misidentified as another yeast when relying on traditional biochemical methods. CDC is aware of one isolate of *C. auris* that was detected in the United States in 2013 as part of ongoing surveillance. Experience outside the United States suggests that *C. auris* has high potential to cause outbreaks in healthcare facilities. Given the occurrence of *C. auris* in nine countries on four continents since 2009, CDC is alerting U.S. healthcare facilities to be on the lookout for *C. auris* in patients.

**Background**

*Candida auris* is an emerging multidrug-resistant (MDR) yeast that can cause invasive infections and is associated with high mortality. It was first described in 2009 after being isolated from external ear discharge of a patient in Japan. Since the 2009 report, *C. auris* infections, specifically fungemia, have been reported from South Korea, India, South Africa, and Kuwait. Although published reports are not available, *C. auris* has also been identified in Colombia, Venezuela, Pakistan, and the United Kingdom.

It is unknown why *C. auris* has recently emerged in so many different locations. Molecular typing of strains performed by CDC suggests isolates are highly related within a species and have high discrimination potential. The routine use of antifungals with *C. auris* based on previous susceptibility data could contribute to the widespread emergence of these infections. CDC continues to work with public health agencies to understand the full extent of this threat and to inform clinicians on the best practices for managing these infections.
C. auris in the US

- As of August 31, we had heard about 7 cases
- All retrospectively found except for 1
12 cases reported by October 2016

CDC Alert

Clinical

Number of cases

May 2013
Sep 2015
Jan 2016
Feb 2016
Mar 2016
Apr 2016
May 2016
Jun 2016
Jul 2016
Aug 2016
Sep 2016
Oct 2016
Nov 2016
Dec 2016
Clinical *C. auris* cases by date
May 2013–May 2017
(n=86)
Epidemiologic Characteristics of US Cases

- 75% of isolates from blood
- Median age: 70, most recently, a case in a neonate
- Multiple underlying medical conditions and indwelling devices
  - Tracheostomy tube, central venous catheter, gastrostomy tube
- Extensive healthcare exposure (acute care hospitals, LTACHs, nursing homes with ventilator units)
- ~30% 30-day mortality
Map of US C. auris cases
Does the US have its own strain?
Evidence for Transmission

Clusters at both hospitals and long-term care facilities

Several patients received care at same hospital

Several patients at same long-term acute care hospital
Three cases with recent travel

- Patient transferred directly from a South African hospital with *C. auris* wound infection.
- Patient with *C. auris* in the urine in 2017; look back revealed he was transferred directly from a Venezuelan hospital with *C. auris* BSI in 2015.
- Patient with recent history of hospitalization in Pakistan, had +urine culture with *C. auris*. 
Multiple introductions of *C. auris* followed by local transmission
Transmission of Candida?
C. auris colonizes skin and other body sites
C. auris found on multiple surfaces in rooms
Close contacts get colonized with *C. auris*

- N=8
- (central line tip)

- N=9

- N=12
- (blood)
What Could Account for Transmission?

- Colonizes patients (and colonized patients are asymptomatic—so can go undetected)
- Persists for >4 weeks on plastic surfaces
- Quaternary ammonium compounds inadequate for disinfection
United States antifungal resistance

- **Illinois**
  - Pan susceptible

- **New Jersey**
  - All fluconazole resistant, one echinocandin resistant, some amphotericin B resistant

- **New York**
  - All fluconazole resistant, one echinocandin resistant, some amphotericin B resistant

- **Oklahoma**
  - Fluconazole and echinocandin resistant
Is it truly an MDR organism?

- MICs for 340 isolates collected worldwide
- 75% of isolates resistant to at least one class of antifungal
- 20% of isolates resistant to two classes of antifungal
- 3 isolates pan resistant
A Paradigm Shift in thinking about *Candida* infections

- Capable of serious infections
- Antifungal resistance is the norm
- Thrives on skin
- Contaminates the environment

CAN SPREAD IN HEALTHCARE SETTINGS
Controlling the spread of *C. auris*

- **IDENTIFY**
- **TREAT**
- **INFECTION CONTROL**
Challenges with identification

- *C. auris* can be misidentified as
  - *Candida haemulonii*
  - *Candida famata*
  - *Candida sake*
  - *Candida catenulate*
  - *Candida guilliermondii*
  - *Candida lusitaniae*
  - *Rhodotorula glutinis,*
  - *Candida* spp. after a validated method of *Candida* identification attempted.

*C. auris* can be correctly identified using MALDI-TOF and DNA sequencing.
Candida auris is difficult to identify

Candida auris is difficult to identify

RUO with Saramis Ver 4.14
Challenges with identification

- 30% of clinical cases in the U.S. have been from non-bloodstream isolates (urine, bile, wounds, etc)
- Isolates from non-sterile sites may not be worked up to species level
  - Though no treatment may be needed, infection control is needed if *C. auris*
Challenges with detecting colonized individuals

Important because infection control measures are needed
Salt Sab Dex Broth with Chloramphenicol and Gentamicin

10% Saline

Temp 40 C
Enrichment broth

Cloudy (right) = positive

CHROMagar

C. auris appears pink
Working with *C. auris* in the lab

At the CDC reference laboratory

- Gloves and gowns are mandatory!
- We work in a biological safety cabinet
- We clean with bleach after working with *C. auris* or a potential *C. auris*
Treatment

- Echinocandins are first line
- Resistance can be problematic
  - Some echinocandin resistant isolates
  - At least one case with documented development of echinocandin resistance on treatment
- Close monitoring of patient needed
Recommended Infection Control Practices

- Standard and Contact Precautions
- Single room
- Hand hygiene
- Daily and terminal cleaning with *Clostridium difficile* claim
- Contact tracing
Take home points:

*Candida auris* poses a unique Public Health threat

- Can be difficult to identify
- Multidrug-resistant (possibly even to all major antifungal drugs)
- Spreads in healthcare settings
- Persists in the environment
Acknowledgements CDC Mycotic Diseases

- Brendan Jackson
- Ana Litvintseva
- Rory Welsh
- Nancy Chow
- Lalitha Gade
- Beth Berkow
- Tom Chiller
- Kizee Etienne
- Sharon Tsay
- Paige Armstrong

- Ngoc Le
- Joyce Peterson
- Alex Bandea
- Diego Caceres
- Shirley McClinton
- Randy Kuykendall
- Karlyn Beer

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Acknowledgements

International
- Anuradha Chowdhary
- Nelesh Govender
- Jacques Meis
- Joveria Farooki
- Belinda Calvo
- Mariana Castanheira
- Arnaldo Colombo
- Kauser Jabeen
- Ronen Ben Ami

Departments of Health
- New York
- Chicago
- Illinois
- New Jersey
- Massachusetts
- Maryland
- Indiana
- Oklahoma

CDC DHQP
- Alex Kallen
- Rachel Slayton
- Bola Ogundimu
- Janet Glowicz

Special thank you to everyone that continues to notify CDC and SPHLs about possible cases

candidaauris@cdc.gov
Thank you! Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Candida auris: Surveillance and Reporting

• Be aware of resources for identifying C. auris and implement infection control measures to prevent spread

• Report possible C. auris or isolates of C. haemulonii and Candida spp. that cannot be identified after routine testing to your local health department and the HAI program, at HAIProgram@cdph.ca.gov.

• For questions regarding fungal diagnostic testing services at CDPH MDL, contact Dr. Linlin Li at Linlin.Li@cdph.ca.gov.
Questions?

The HAI Program is available for consultation. Contact us by email:

HAIProgram@cdph.ca.gov